

The listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1-16. (Canceled)

17. (Currently Amended) A method for the treatment of rheumatoid arthritis ~~a disease other than cancer mediated by p38~~ which comprises administering to a patient in need thereof an effective amount of a compound of formula I or a pharmaceutically acceptable salt thereof



wherein B is phenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl substituted by -Y-Ar; and is optionally substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and X<sub>n</sub>,

wherein n is 0-3 and each X is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5'</sup>, -C(O)R<sup>5</sup>, -NO<sub>2</sub>, -OR<sup>5</sup>, -SR<sup>5</sup>, -NR<sup>5</sup>R<sup>5'</sup>, -NR<sup>5</sup>C(O)OR<sup>5'</sup>, -NR<sup>5</sup>C(O)R<sup>5'</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, phenyl, pyridinyl, naphthyl, isoquinolinyl, quinolinyl, up to per halo-substituted C<sub>1</sub>-C<sub>10</sub> alkyl, up to per halo-substituted C<sub>2</sub>-C<sub>10</sub> alkenyl, up to per halo-substituted C<sub>1</sub>-C<sub>10</sub> alkoxy, up to per halo-substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl, and

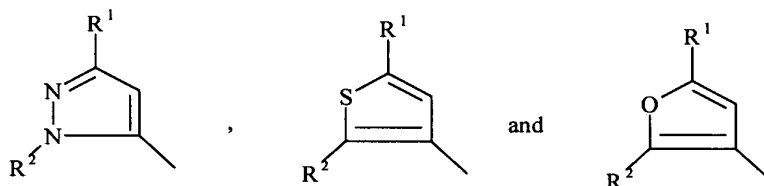
wherein R<sup>5</sup> and R<sup>5'</sup> are independently selected from H, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, up to per-halosubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, up to per-halosubstituted C<sub>2</sub>-C<sub>10</sub> alkenyl and up to per-halosubstituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl,

wherein Y is -O-, -S-, -N(R<sup>5</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -NR<sup>5</sup>C(O)NR<sup>5</sup>NR<sup>5'</sup>-, -NR<sup>5</sup>C(O)-, -C(O)NR<sup>5</sup>-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>5</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-, -CHX<sup>a</sup>, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>5</sup>)(CH<sub>2</sub>)<sub>m</sub>-,

m = 1-3, and X<sup>a</sup> is halogen; and

Ar is phenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl, optionally substituted by halogen up to per-halosubstitution and optionally substituted by  $Z_{n1}$ , wherein  $n1$  is 0 to 3 and each Z is independently selected from the group consisting of  $-\text{CN}$ ,  $=\text{O}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^5$ ,  $-\text{C}(\text{O})-\text{NR}^5$ ,  $-\text{NO}_2$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{R}^5$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^5$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^5$ ,  $-\text{SO}_2\text{R}^5$ ,  $\text{SO}_2\text{NR}^5\text{R}^5$ ,  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{C}_1\text{-C}_{10}$  alkoxy,  $\text{C}_3\text{-C}_{10}$  cycloalkyl, up to per halo-substituted  $\text{C}_1\text{-C}_{10}$  alkyl, and up to per halo-substituted  $\text{C}_3\text{-C}_{10}$  cycloalkyl, and

wherein A is a heteroaryl selected from the group consisting of



wherein  $\text{R}^1$  is selected from the group consisting of  $\text{C}_3\text{-C}_{10}$  alkyl,  $\text{C}_3\text{-C}_{10}$  cycloalkyl, up to per-halosubstituted  $\text{C}_1\text{-C}_{10}$  alkyl and up to per-halosubstituted  $\text{C}_3\text{-C}_{10}$  cycloalkyl,

wherein  $\text{R}^2$  is  $\text{C}_6\text{-C}_{14}$  aryl,  $\text{C}_3\text{-C}_{14}$  heteroaryl, or substituted  $\text{C}_6\text{-C}_{14}$  aryl or substituted  $\text{C}_3\text{-C}_{14}$  heteroaryl,

wherein if  $\text{R}^2$  is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and  $\text{V}_n$ ,

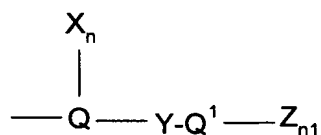
wherein  $n = 0\text{-}3$  and each V is independently selected from the group consisting of  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^5$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{R}^5$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{OC}(\text{O})\text{NR}^5\text{R}^5$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^5$ ,  $-\text{SO}_2\text{R}^5$ ,  $-\text{SOR}^5$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^5$ ,  $-\text{NO}_2$ ,  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{C}_3\text{-C}_{10}$  cycloalkyl,  $\text{C}_6\text{-C}_{14}$  aryl,  $\text{C}_3\text{-C}_{13}$  heteroaryl,  $\text{C}_7\text{-C}_{24}$  alkaryl,  $\text{C}_4\text{-C}_{24}$  alkheteroaryl, substituted  $\text{C}_1\text{-C}_{10}$  alkyl, substituted  $\text{C}_3\text{-C}_{10}$  cycloalkyl, substituted  $\text{C}_6\text{-C}_{14}$  aryl, substituted  $\text{C}_3\text{-C}_{13}$  heteroaryl, substituted  $\text{C}_7\text{-C}_{24}$  alkaryl and substituted  $\text{C}_4\text{-C}_{24}$  alkheteroaryl,

where V is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution,  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^5$ ,  $-\text{NR}^5\text{R}^5$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^5$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^5$  and  $-\text{NO}_2$ ,

wherein R<sup>5</sup> and R<sup>6</sup> are each independently as defined above.

18. (Currently Amended) A method as in claim 17 wherein R<sup>2</sup> is phenyl ~~[[5]]~~ or substituted phenyl, ~~pyridinyl or substituted pyridinyl~~.

19. (Currently Amended) A method of claim 17, wherein B is



wherein

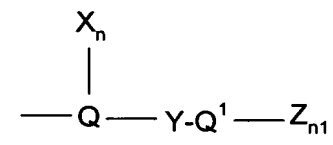
Y is as defined in claim 17,

Q and Q<sup>1</sup> are independently selected from the group consisting of phenyl, pyridinyl, naphthyl, pyrimidinyl, quinoline, isoquinoline, imidazole and benzothiazolyl, optionally substituted by halogen, up to per-halo substitution, ~~and~~

Z and X are independently selected from the group consisting of -R<sup>6</sup>, -OR<sup>6</sup> and -NHR<sup>7</sup>, wherein R<sup>6</sup> is hydrogen, C<sub>1</sub>-C<sub>10</sub>-alkyl or C<sub>3</sub>-C<sub>10</sub>-cycloalkyl and R<sup>7</sup> is selected from the group consisting of hydrogen, C<sub>3</sub>-C<sub>10</sub>-alkyl, and C<sub>3</sub>-C<sub>6</sub>-cycloalkyl wherein R<sup>6</sup> and R<sup>7</sup> can be substituted by halogen or up to per-halosubstitution, and

n and n1 are, each independently 0-3.

20. (Currently Amended) A method as in claim ~~17~~ 19, wherein B is



wherein

Q is phenyl,

Q<sup>1</sup> is phenyl or pyridinyl,

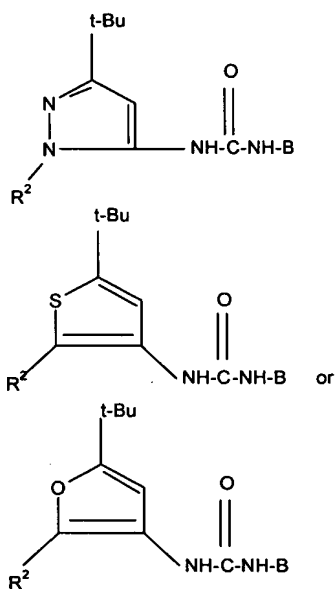
Y is -O-, -S- or -CH<sub>2</sub>, ~~and~~

X and Z are independently Cl, F, CF<sub>3</sub>, NO<sub>2</sub> or CN,

n and n1 are, each independently 0-3, and

wherein Q and Q<sup>1</sup> are optionally substituted by one or more Cl and/or F.

21. (Previously Presented) A method as in claim 17, which comprises administering a compound of one of the formulae or a pharmaceutically acceptable salt thereof:



wherein B and R<sup>2</sup> are as defined in claim 17.

22. (Currently Amended) A method as in claim 21, wherein R<sup>2</sup> is phenyl, ~~pyridinyl, or substituted phenyl or substituted pyridinyl.~~

23. (Previously Presented) A method as in claim 17, comprising administering an amount of compound of formula I effective to inhibit p38.

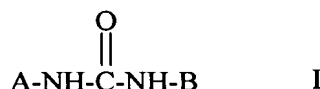
24. (Previously Presented) A method as in claim 17, wherein the compound of formula I displays p38 activity (IC<sub>50</sub>) better than 10μM as determined by an in-vitro kinase assay.

25. (Canceled)

26. (Currently Amended) A method according to claim 30 47, wherein R<sup>1</sup> is t-butyl.

27-29. (Canceled)

30. (Currently Amended) A method ~~according to claim 17, wherein the disease is for the treatment of Crohn's disease,~~ rheumatoid arthritis, osteoarthritis, osteoporosis, asthma, septic shock, inflammatory bowel disease, or the result of host-versus-graft reactions which comprises administering to a patient in need thereof an effective amount of a compound of formula I or a pharmaceutically acceptable salt thereof



wherein B is phenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl substituted by -Y-Ar; and is optionally substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and X<sub>n</sub>,

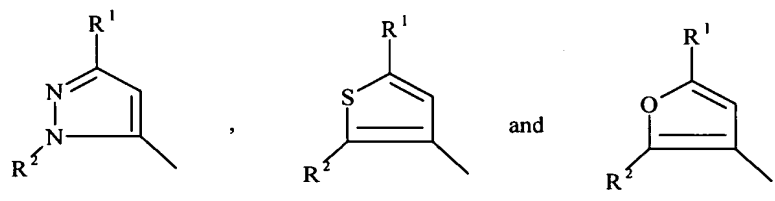
wherein n is 0-3 and each X is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5'</sup>, -C(O)R<sup>5</sup>, -NO<sub>2</sub>, -OR<sup>5</sup>, -SR<sup>5</sup>, -NR<sup>5</sup>R<sup>5'</sup>, -NR<sup>5</sup>C(O)OR<sup>5</sup>, -NR<sup>5</sup>C(O)R<sup>5'</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, phenyl, pyridinyl, naphthyl, isoquinolinyl, quinolinyl, up to per halo-substituted C<sub>1</sub>-C<sub>10</sub> alkyl, up to per halo-substituted C<sub>2</sub>-C<sub>10</sub> alkenyl, up to per halo-substituted C<sub>1</sub>-C<sub>10</sub> alkoxy, up to per halo-substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl, and

wherein R<sup>5</sup> and R<sup>5'</sup> are independently selected from H, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, up to per-halosubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, up to per-halosubstituted C<sub>2</sub>-C<sub>10</sub> alkenyl and up to per-halosubstituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl,

wherein Y is -O-, -S-, -N(R<sup>5</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -NR<sup>5</sup>C(O)NR<sup>5</sup>NR<sup>5'</sup>-, -NR<sup>5</sup>C(O)-, -C(O)NR<sup>5</sup>-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>5</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-, -CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>5</sup>)(CH<sub>2</sub>)<sub>m</sub>-,

m = 1-3, and X<sup>a</sup> is halogen; and

Ar is phenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl, optionally substituted by halogen up to per-halosubstitution and optionally substituted by  $Z_{n1}$ , wherein  $n1$  is 0 to 3 and each Z is independently selected from the group consisting of  $-CN$ ,  $=O$ ,  $-CO_2R^5$ ,  $-C(O)NR^5R^{5'}$ ,  $-C(O)NR^5$ ,  $-NO_2$ ,  $-OR^5$ ,  $-SR^5$ ,  $-NR^5R^{5'}$ ,  $-NR^5C(O)OR^{5'}$ ,  $-C(O)R^5$ ,  $-NR^5C(O)R^5$ ,  $-SO_2R^5$ ,  $SO_2NR^5R^{5'}$ ,  $C_1-C_{10}$  alkyl,  $C_1-C_{10}$  alkoxy,  $C_3-C_{10}$  cycloalkyl, up to per halo-substituted  $C_1-C_{10}$  alkyl, and up to per halo-substituted  $C_3-C_{10}$  cycloalkyl, and \_\_\_\_\_ wherein A is a heteroaryl selected from the group consisting of



\_\_\_\_\_ wherein  $R^1$  is selected from the group consisting of  $C_3-C_{10}$  alkyl,  $C_3-C_{10}$  cycloalkyl, up to per-halosubstituted  $C_1-C_{10}$  alkyl and up to per-halosubstituted  $C_3-C_{10}$  cycloalkyl,

wherein  $R^2$  is  $C_6-C_{14}$  aryl,  $C_3-C_{14}$  heteroaryl, or substituted  $C_6-C_{14}$  aryl or substituted  $C_3-C_{14}$  heteroaryl,

wherein if  $R^2$  is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and  $V_n$ ,

\_\_\_\_\_ wherein  $n = 0-3$  and each V is independently selected from the group consisting of  $-CN$ ,  $-CO_2R^5$ ,  $-C(O)NR^5R^{5'}$ ,  $-OR^5$ ,  $-SR^5$ ,  $-NR^5R^{5'}$ ,  $-C(O)R^5$ ,  $-OC(O)NR^5R^{5'}$ ,  $-NR^5C(O)OR^{5'}$ ,  $-SO_2R^5$ ,  $-SOR^5$ ,  $-NR^5C(O)R^5$ ,  $-NO_2$ ,  $C_1-C_{10}$  alkyl,  $C_3-C_{10}$  cycloalkyl,  $C_6-C_{14}$  aryl,  $C_3-C_{13}$  heteroaryl,  $C_7-C_{24}$  alkaryl,  $C_4-C_{24}$  alkheteroaryl, substituted  $C_1-C_{10}$  alkyl, substituted  $C_3-C_{10}$  cycloalkyl, substituted  $C_6-C_{14}$  aryl, substituted  $C_3-C_{13}$  heteroaryl, substituted  $C_7-C_{24}$  alkaryl and substituted  $C_4-C_{24}$  alkheteroaryl,

\_\_\_\_\_ where V is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution,  $-CN$ ,  $-CO_2R^5$ ,  $-C(O)R^5$ ,  $-C(O)NR^5R^{5'}$ ,  $-NR^5R^{5'}$ ,  $-OR^5$ ,  $-SR^5$ ,  $-NR^5C(O)R^5$ ,  $-NR^5C(O)OR^{5'}$  and  $-NO_2$ ,

wherein R<sup>5</sup> and R<sup>6</sup> are each independently as defined above.

31. (Currently Amended) A method as in claim 30 1, wherein R<sup>2</sup> is phenyl.

32. (Currently Amended) A method as in claim 30 1, wherein R<sup>2</sup> is a substituted C<sub>6</sub>-C<sub>14</sub> aryl or substituted C<sub>3</sub>-C<sub>14</sub> heteroaryl.